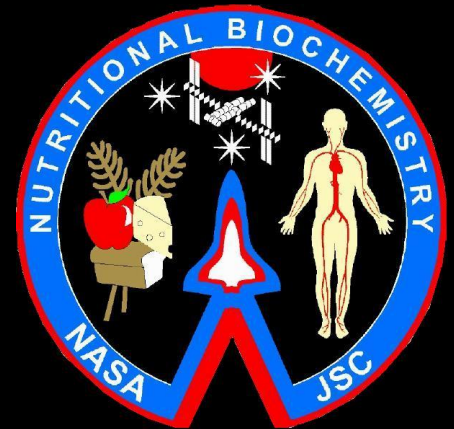


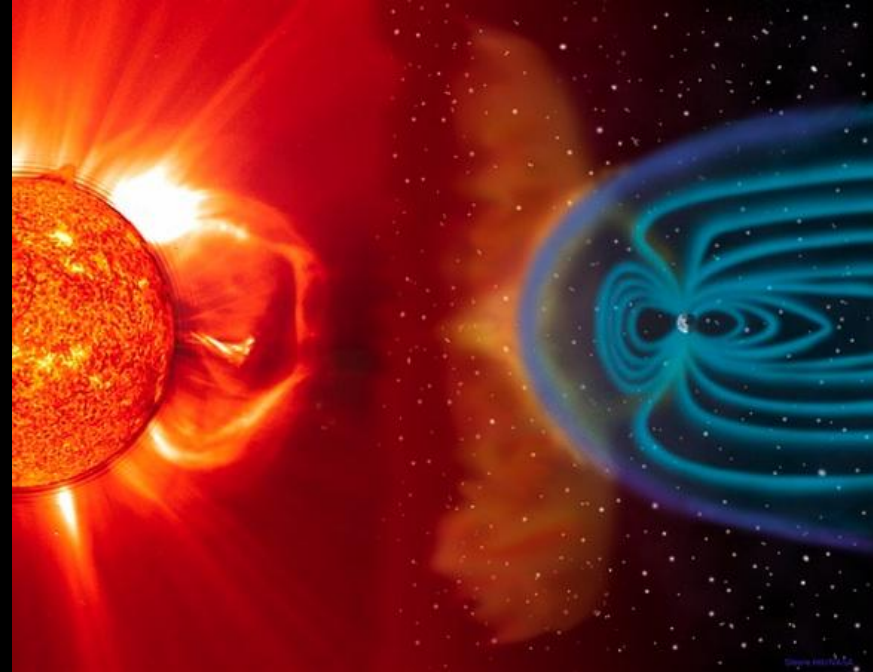
Combined effects of Gamma Radiation and High Dietary Iron on Peripheral Leukocyte Distribution and Function

Brian E. Crucian,
Jennifer L.L. Morgan
Heather A. Quiriarte
Clarence F. Sams
Scott M. Smith
Sara R. Zwart

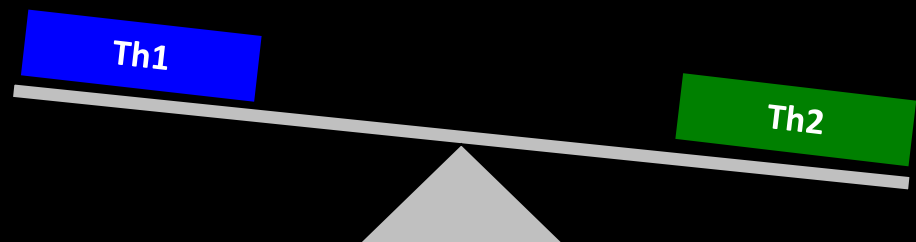
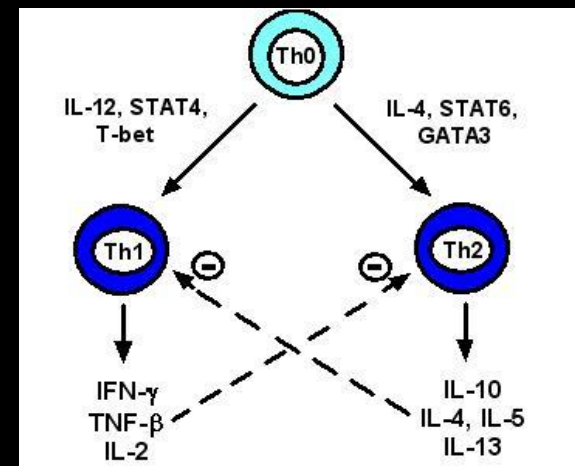
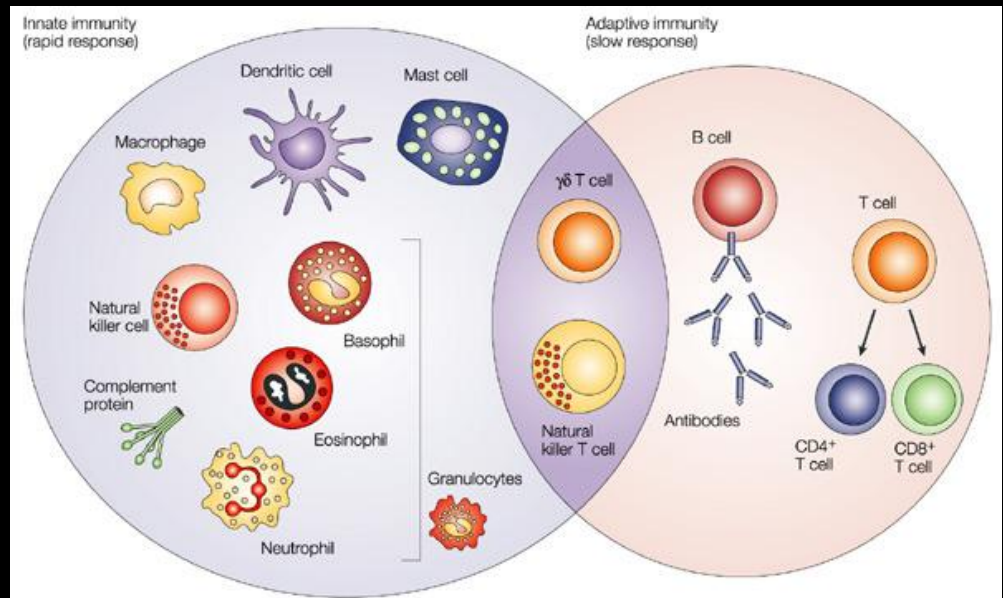
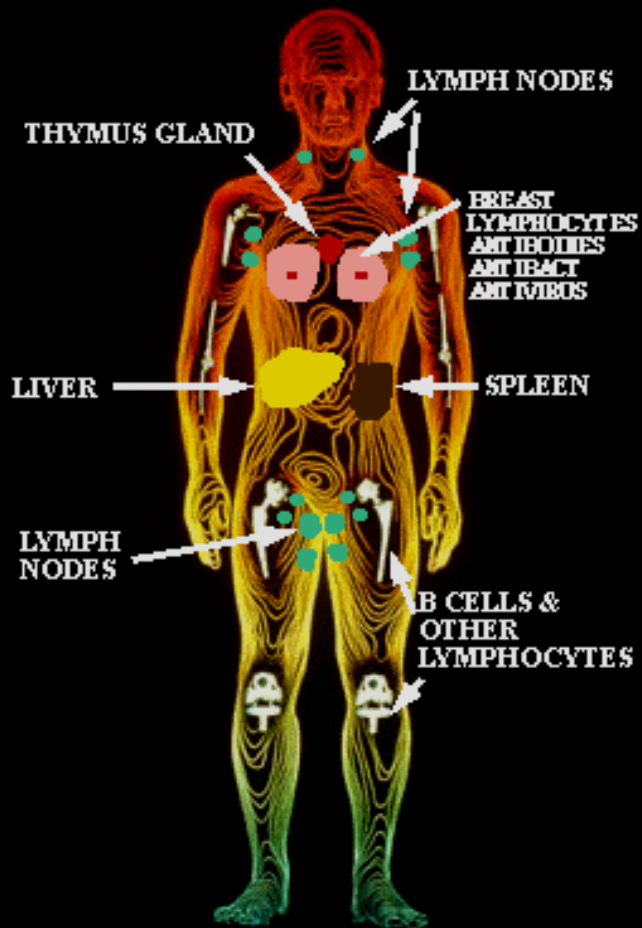


Concept

- Both radiation and increased iron stores can independently increase oxidative damage, resulting in protein, lipid and DNA oxidation.
- Oxidative stress increases the risk of many health problems including cancer, cataracts, and heart disease.
- This study, a subset of a larger interdisciplinary investigation of the combined *effect of iron overload on sensitivity to radiation injury*, monitored immune parameters in the peripheral blood of rats subjected to gamma radiation, high dietary iron or both.
- Specific immune measures consisted of:
 - peripheral leukocyte distribution
 - plasma cytokine levels
 - cytokine production profiles following whole blood mitogenic stimulation

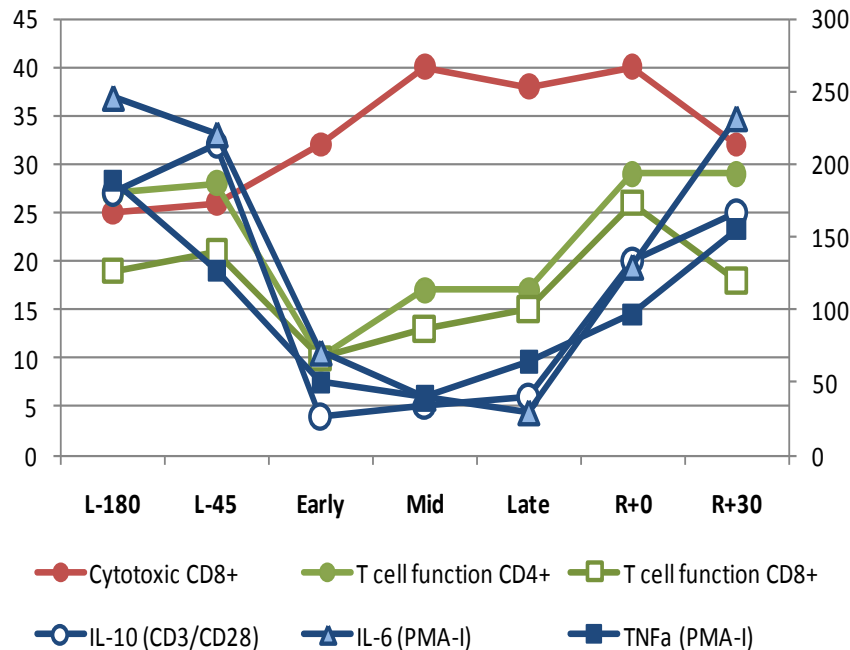


THE IMMUNE SYSTEM

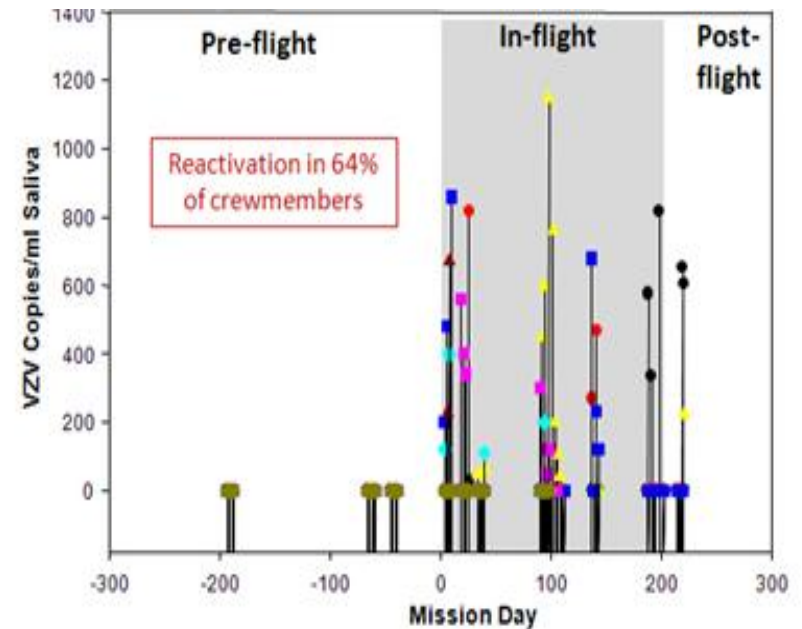


Integrated Immune mid-study long duration data (n=10)

Immune Parameters

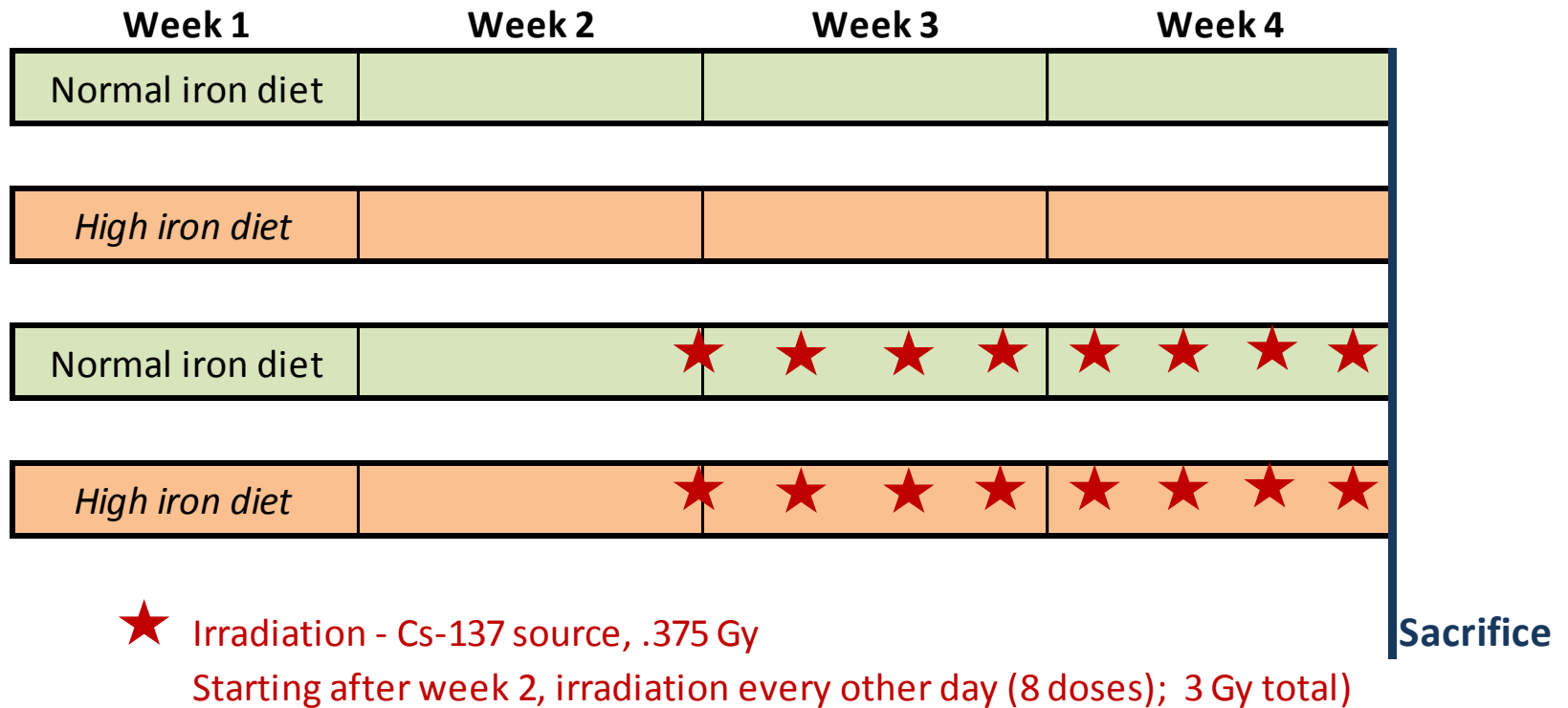


VZV Reactivation



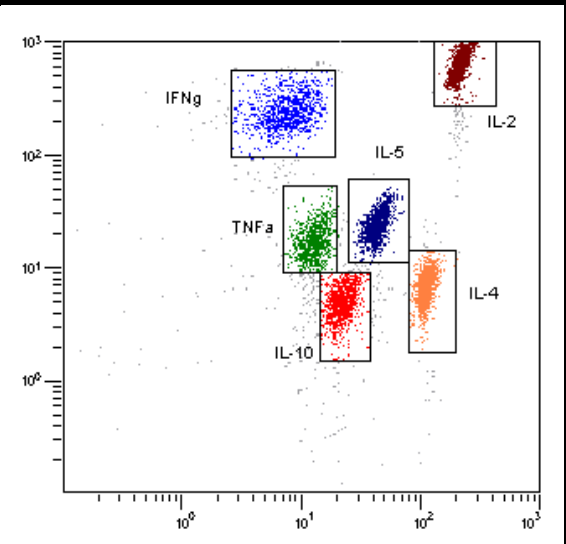
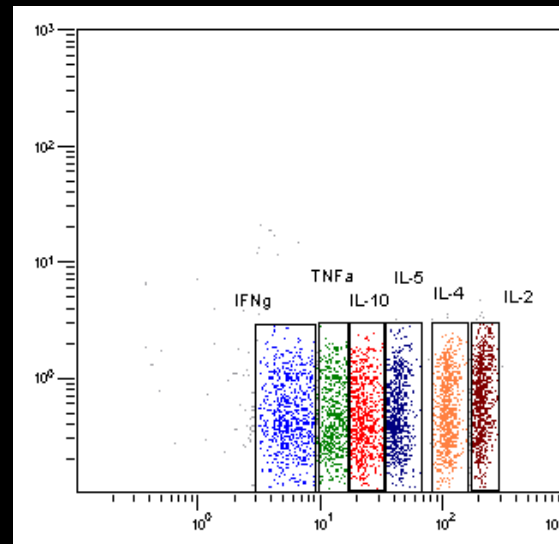
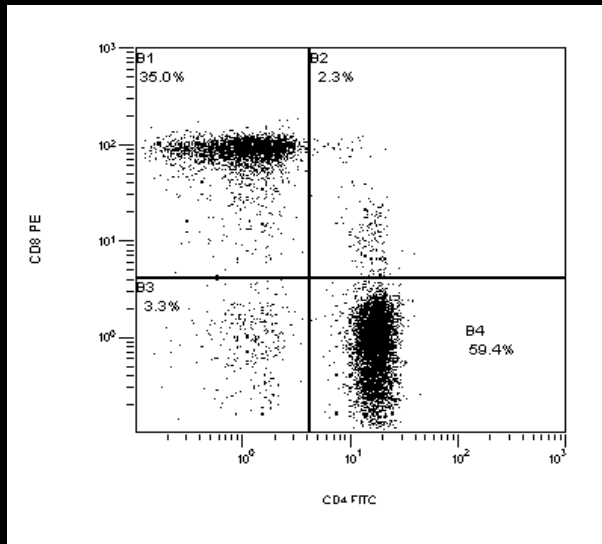
Immune dysregulation during deep space missions has the capacity to synergize with other variables such as oxidative damage or radiation exposure. This would further enhance clinical risk to crewmembers.

Current Study Design

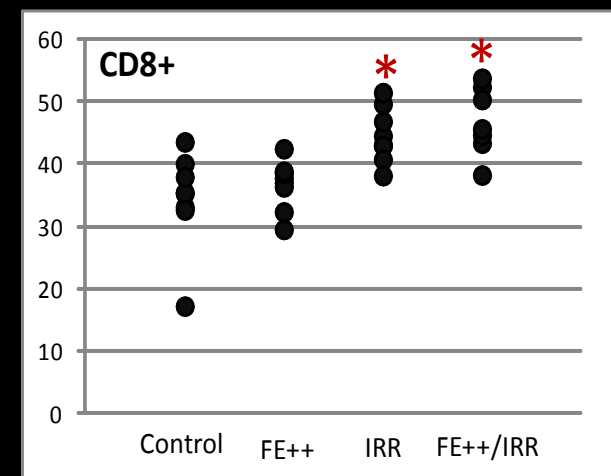
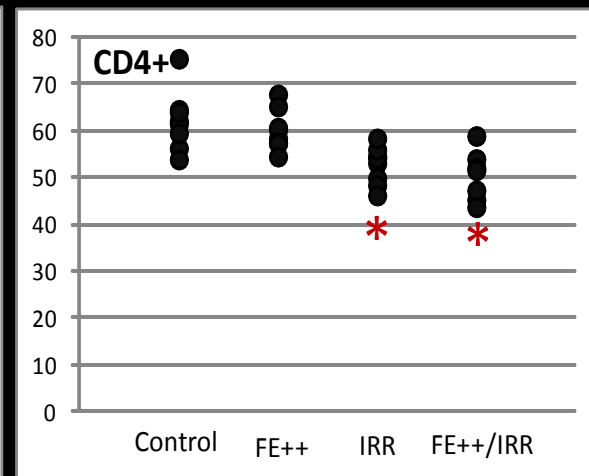
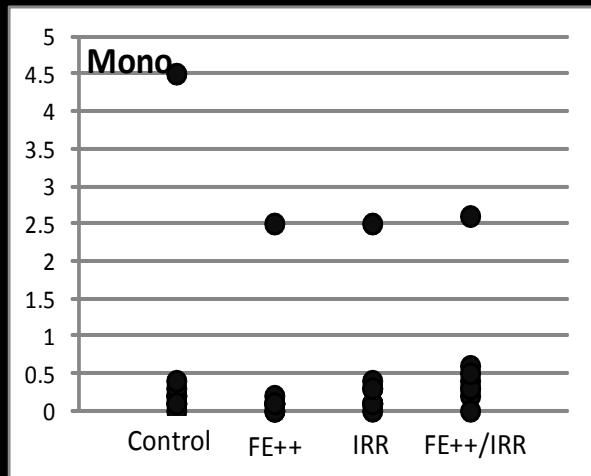
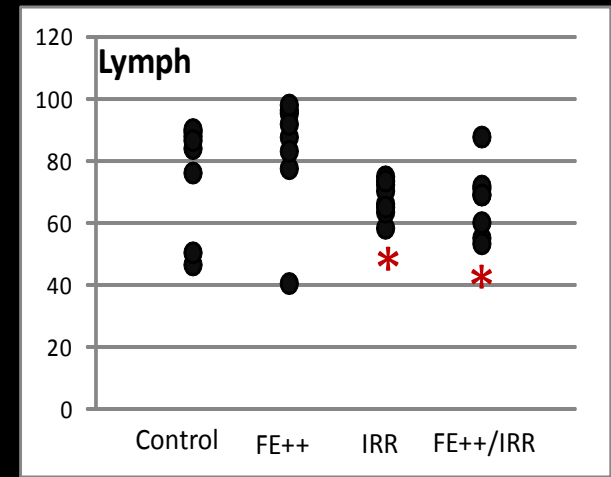
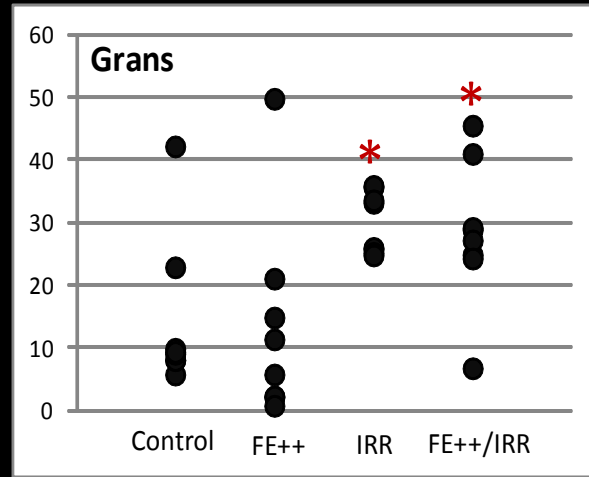
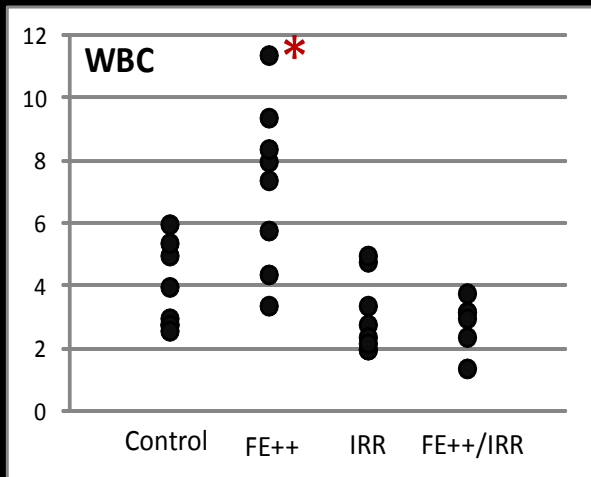


Specific Immunology Assays

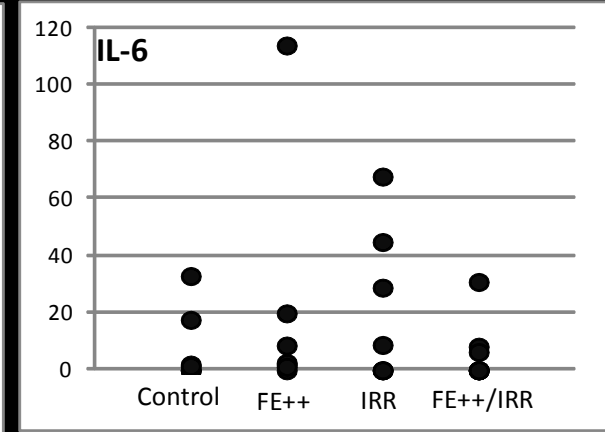
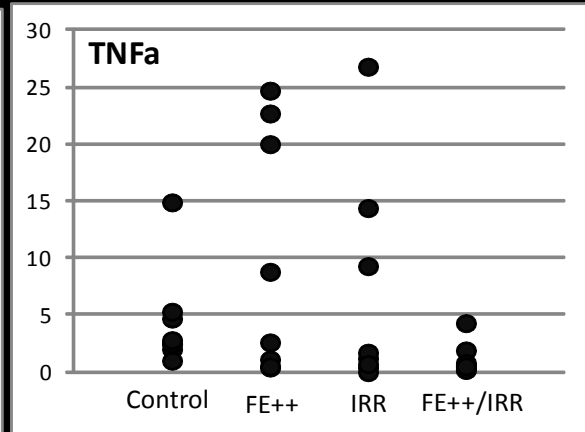
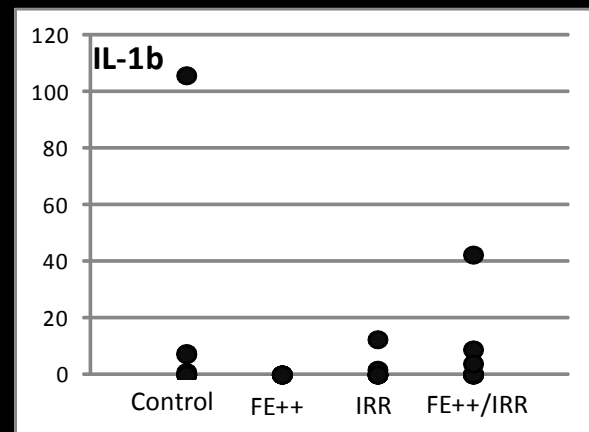
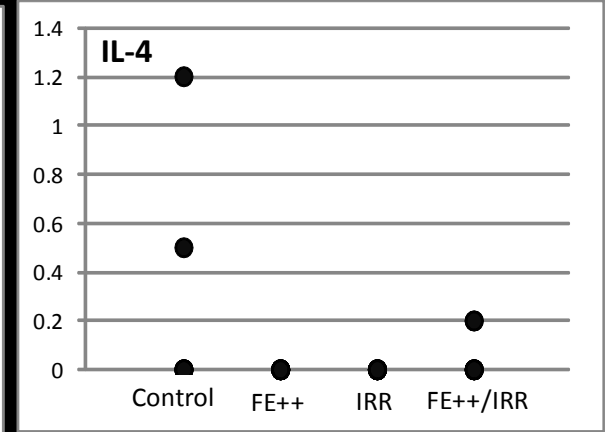
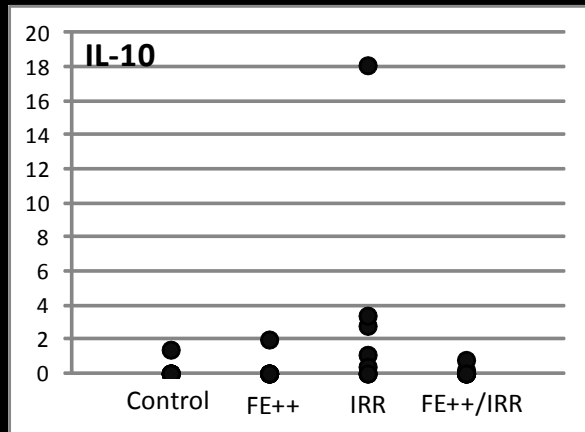
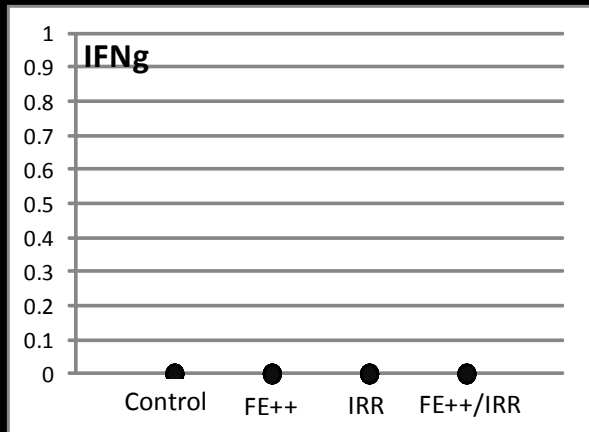
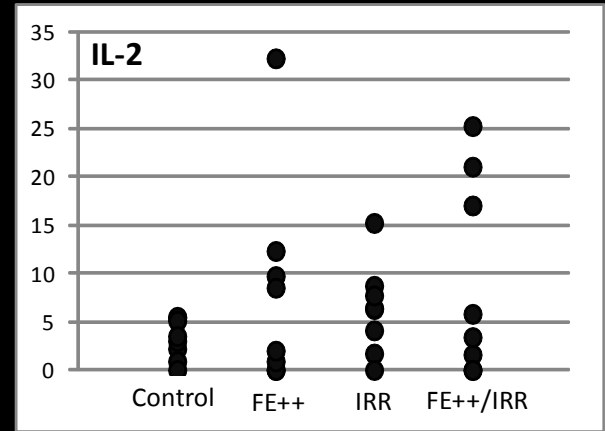
- WBC
- Neutrophil, Lymphocyte, Monocyte
- T cell subsets: CD4+/CD8+ (Flow cytometry)
- Cytokine Profiles (cytometrix bead array)
 - Adaptive immunity: IFNg, IL-10, IL-4, IL-2
 - Innate/inflammatory: TNFa, IL-1b, IL-6)



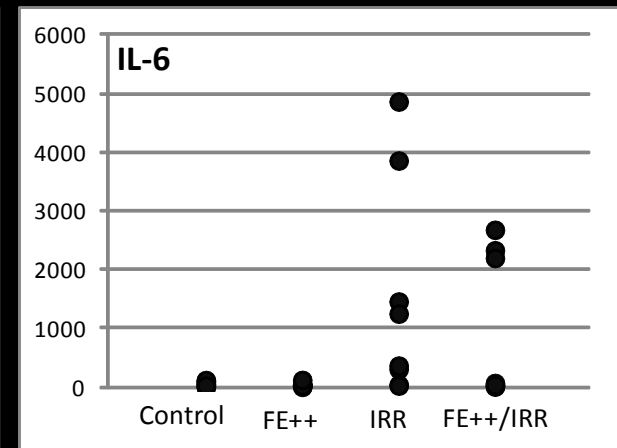
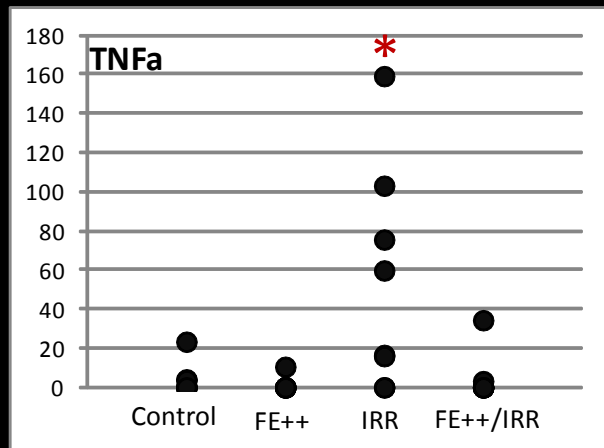
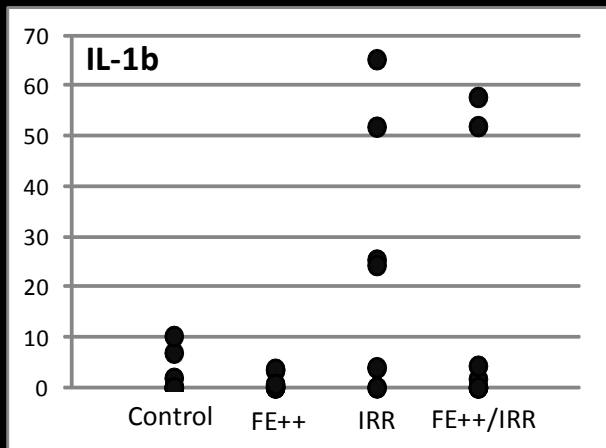
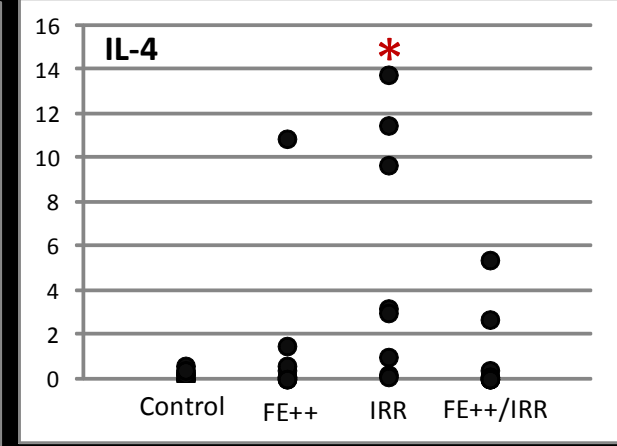
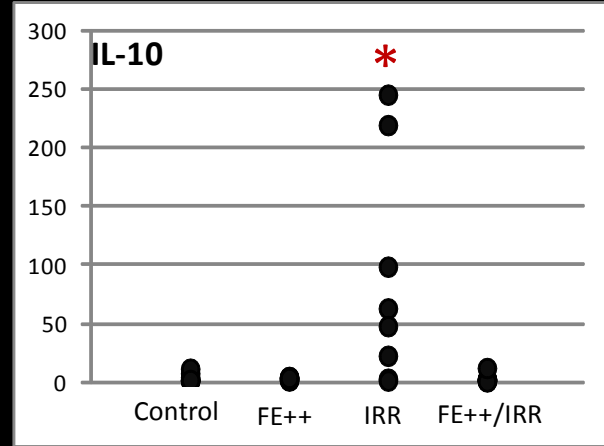
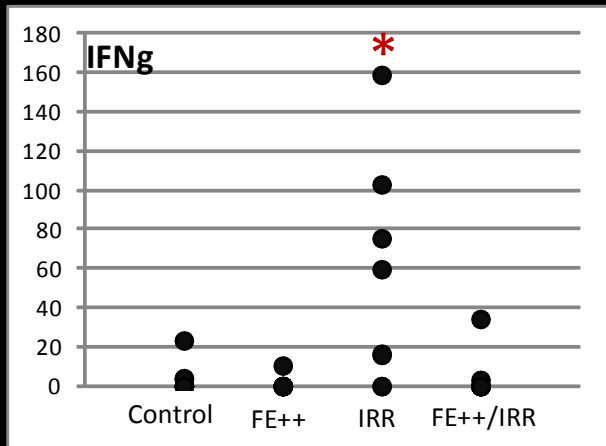
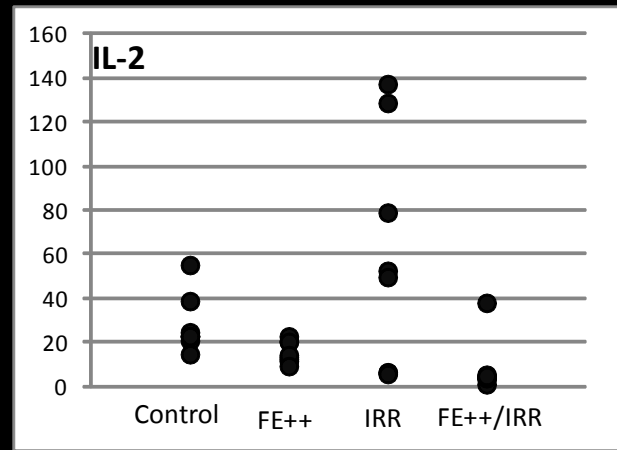
Leukocyte Distribution



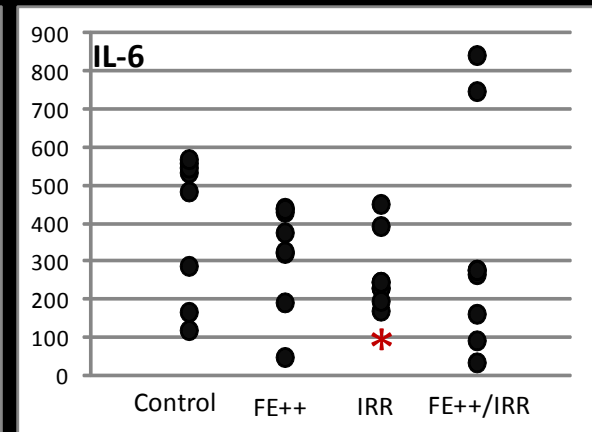
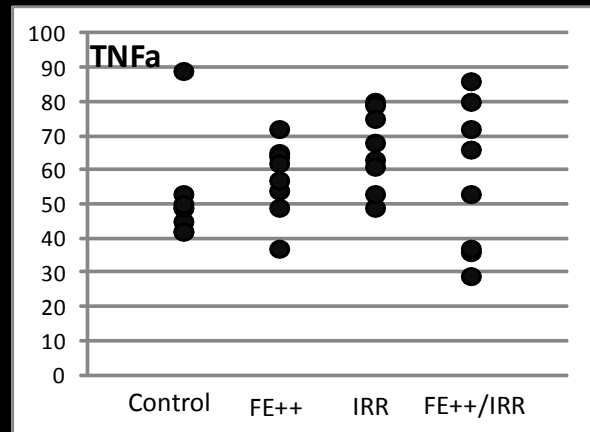
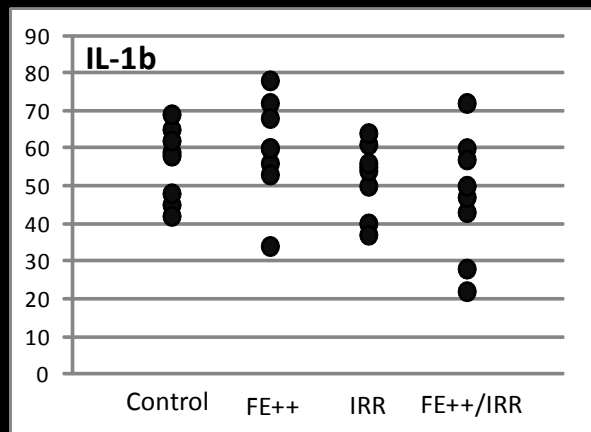
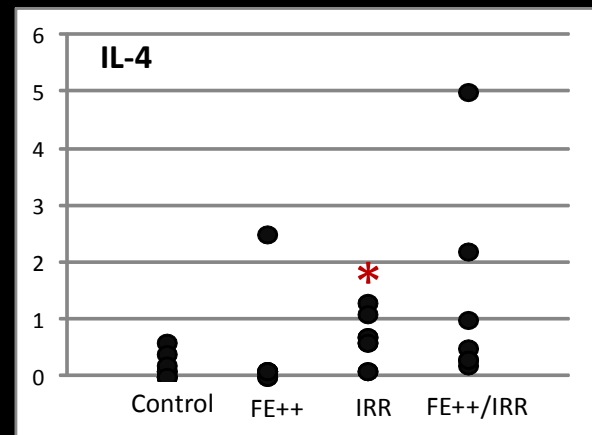
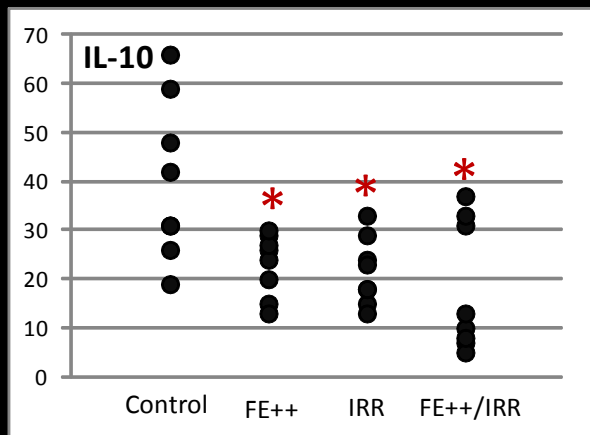
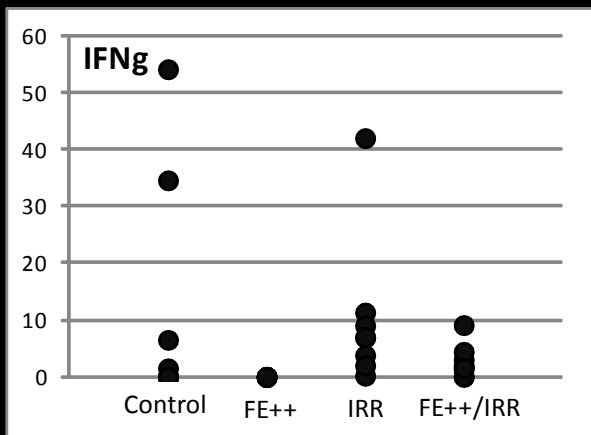
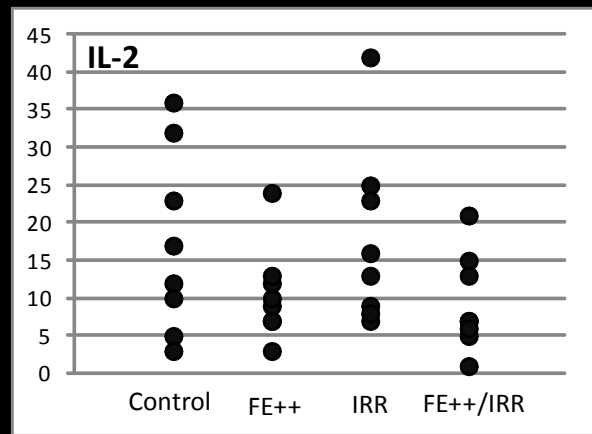
Constitutive Plasma Cytokine Levels



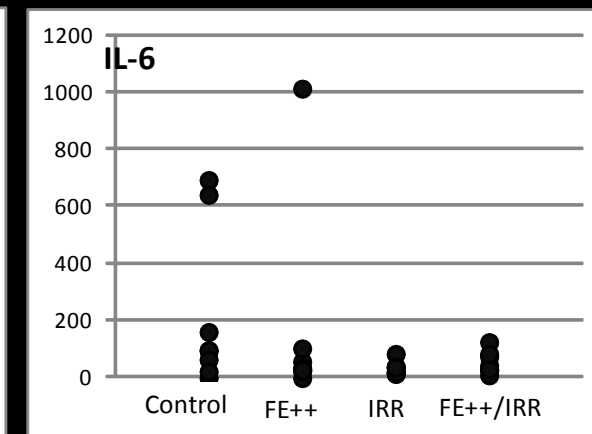
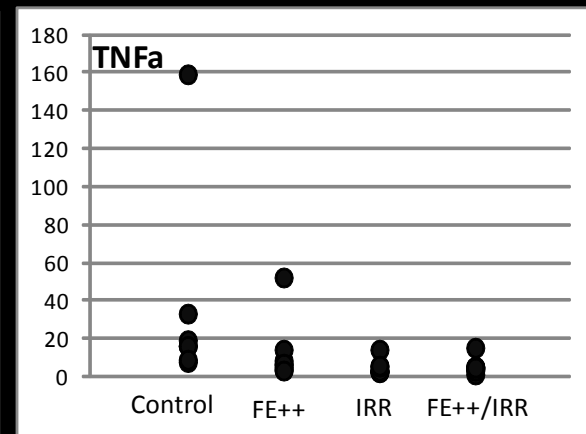
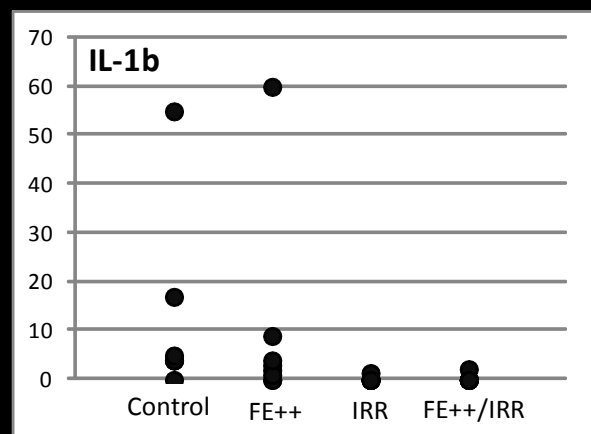
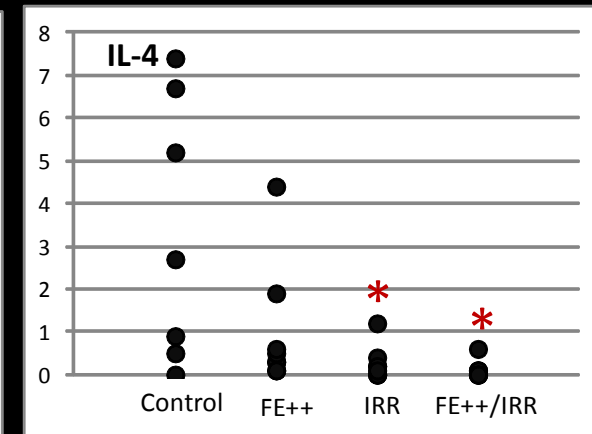
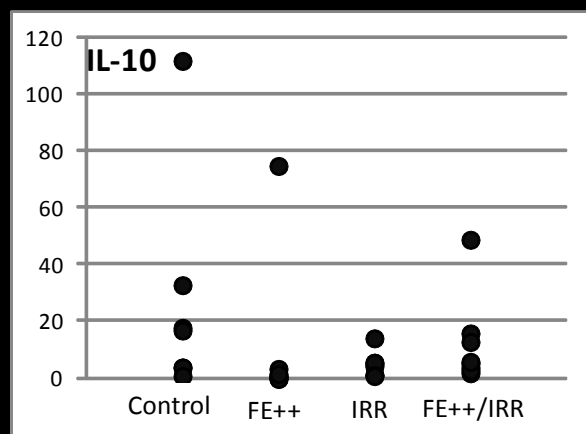
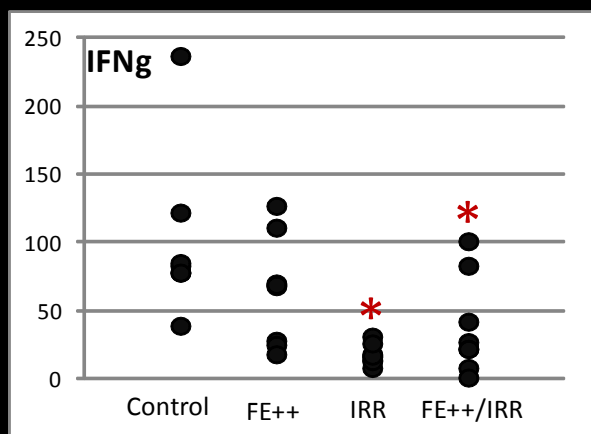
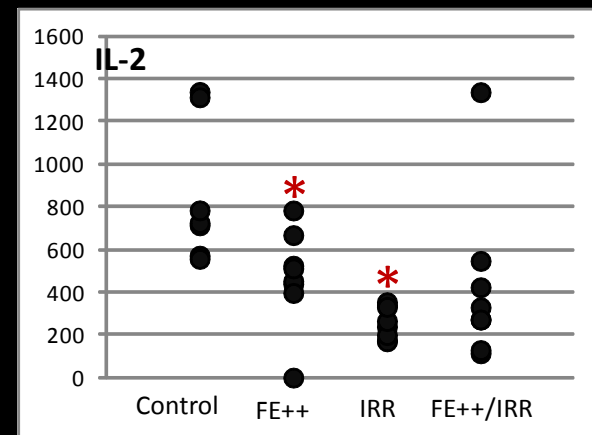
Cytokine Production Profiles (*anti-CD3/28, 48hr*)



Cytokine Production Profiles (anti LPS, 48hr)



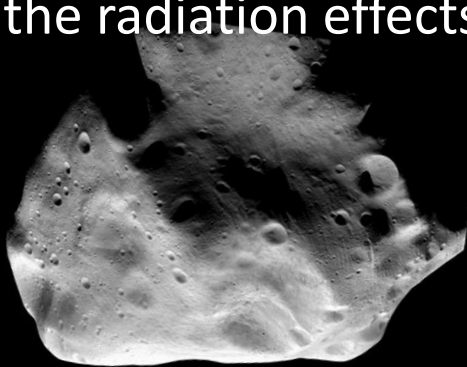
Cytokine Production Profiles (anti PMA-I, 48hr)



Conclusions

(and places we can go...)

- Gamma-radiation treatment: Demonstrable alterations in peripheral leukocyte distribution and leukocyte cytokine production following mitogenic stimulation.
- High iron diet: Resulted in an elevated WBC but with a normal subset distribution; minimal direct immune effects; abrogated some of the radiation-induced functional alterations but not the phenotypic alterations
- Summary: Radiation induced demonstrable changes in peripheral immunity. Generally, the high iron diet did not, yet did abrogate many of the radiation effects.



Lutetia (Rosetta)



Gaspar (Galileo)

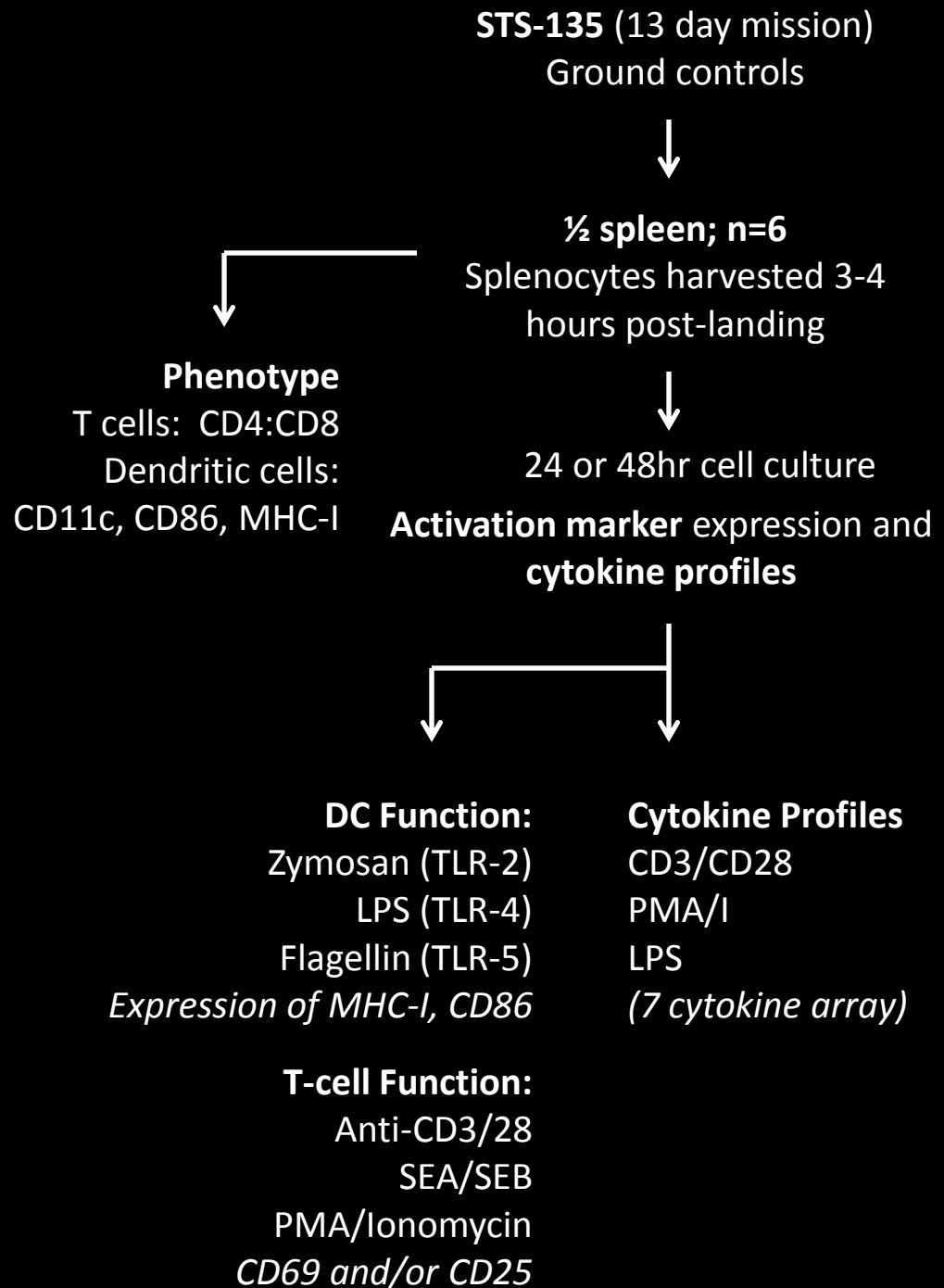


Ida (Galileo)

ALTERED INNATE AND LYMPHOCYTIC IMMUNITY IN MURINE SPLENOCYTES FOLLOWING SHORT-DURATION SPACEFLIGHT

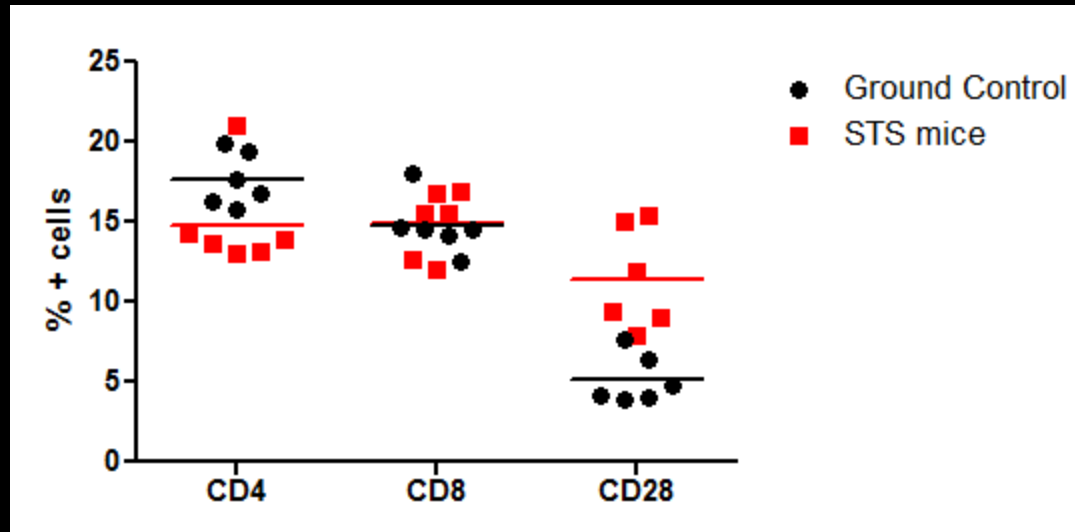
Brian E. Crucian
Shen-An Hwang
Jeffrey K. Actor
Heather Quiriarte
Clarence F. Sams

STS-135 Study Design



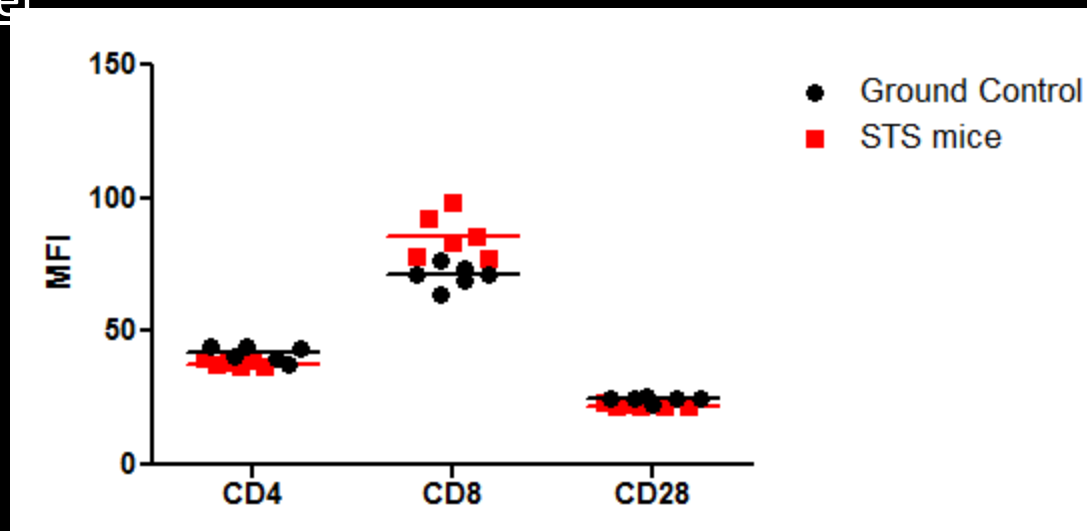
Altered expression of lymphocytic markers post-flight

% positive cells



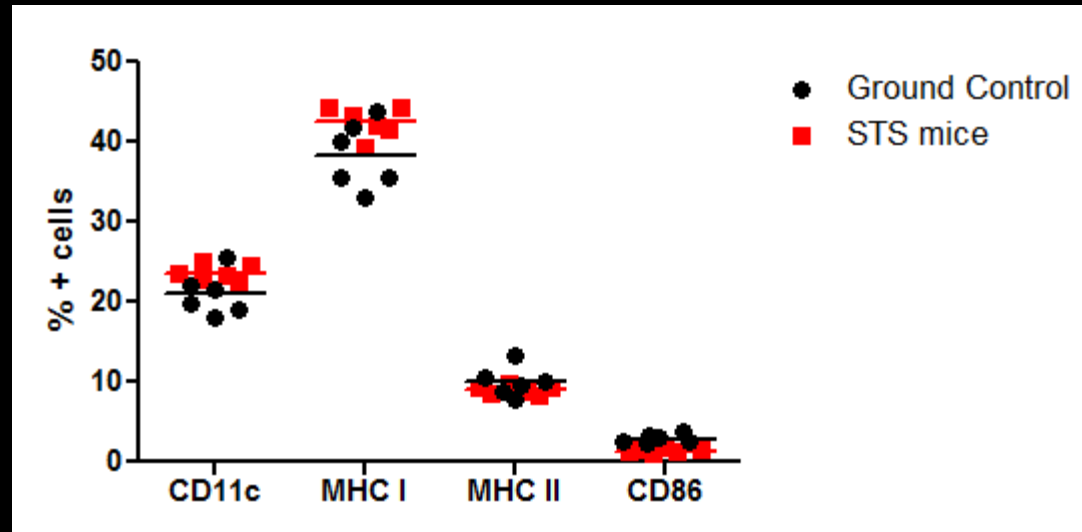
*** = $p < 0.001$

Intensity of marker expression



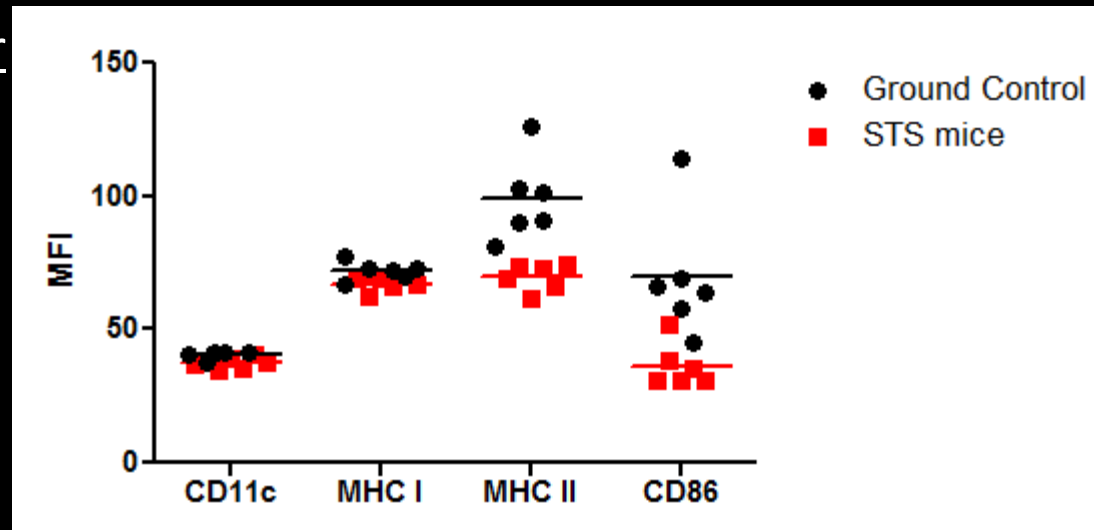
Post-flight splenocytes have decreased expression of antigen presentation and co-stimulatory molecules

% positive cells

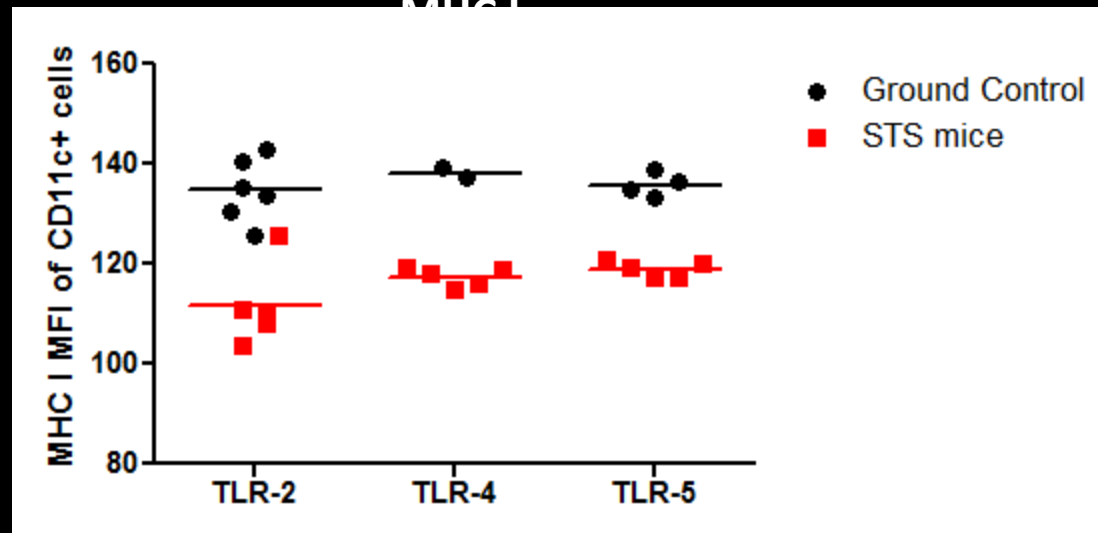


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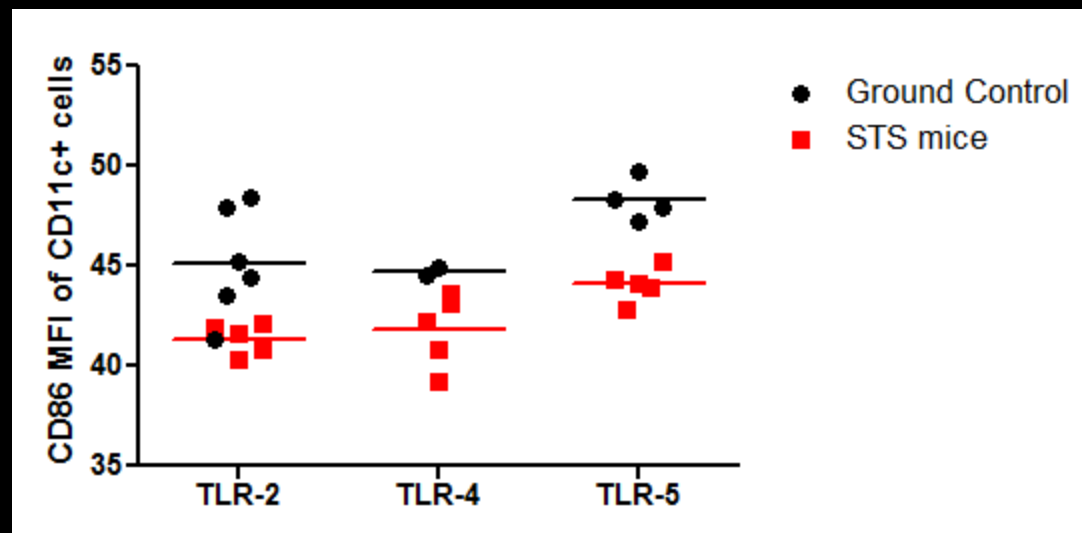
Intensity of marker expression



Post-flight DCs show decreased expression of presentation and co-stimulatory molecules after TLR stimulation

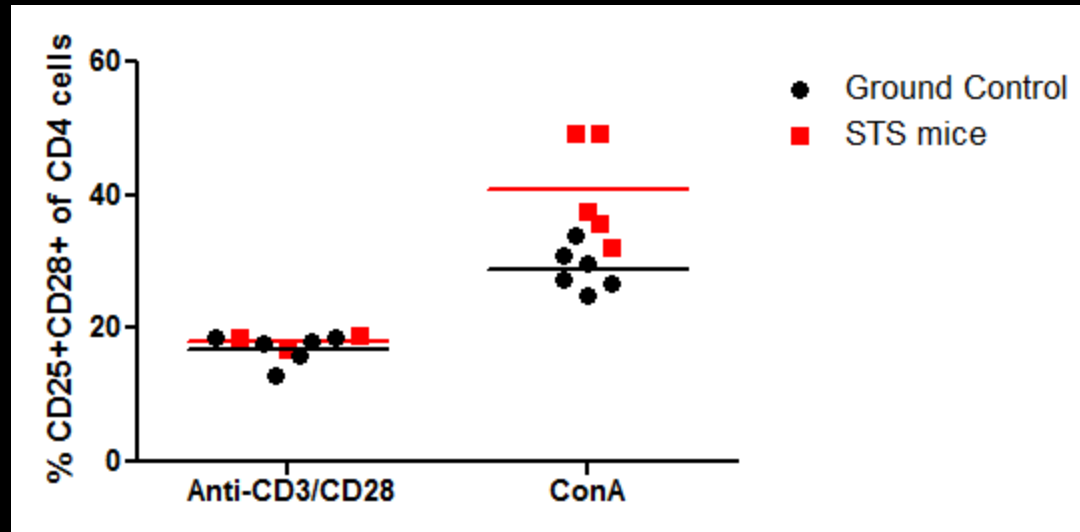


** = $p < 0.01$
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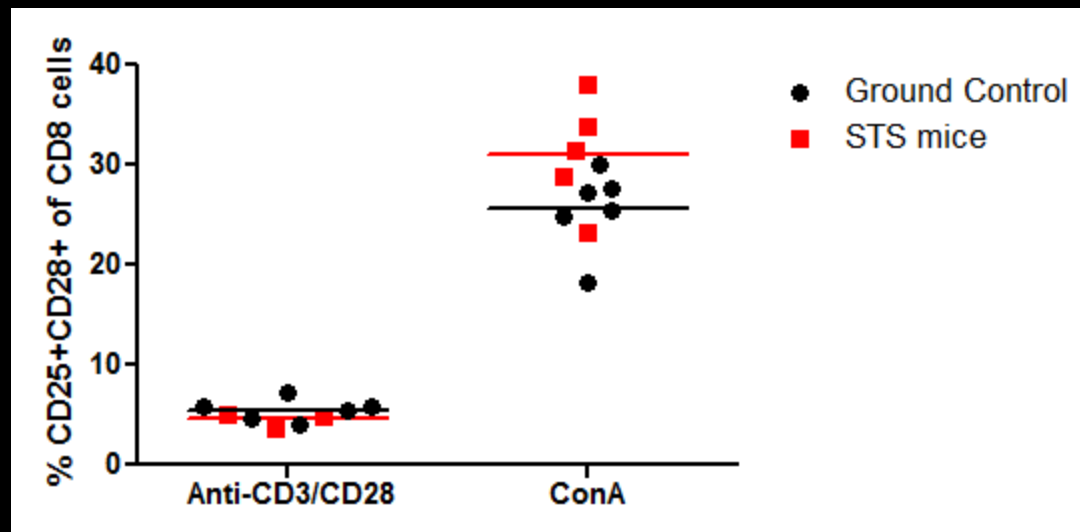


differences in
CD86 observed

Post-flight splenocytes demonstrate increased CD25⁺ in CD4⁺/CD8⁺CD28⁺ cells when stimulation bypasses the 2^o signal



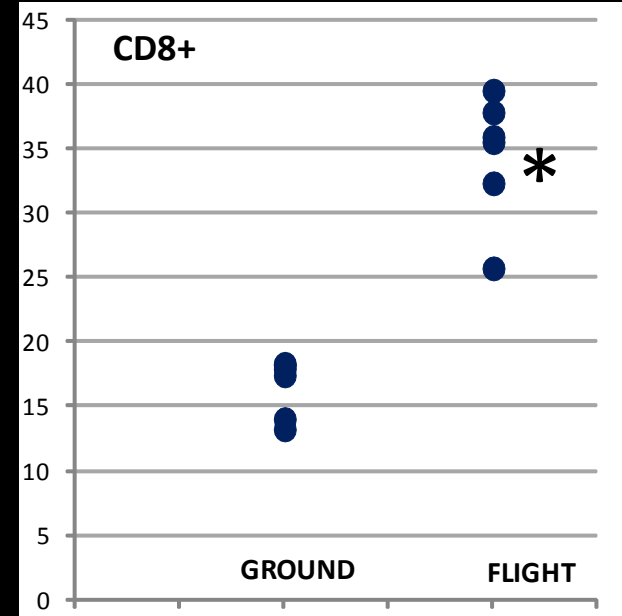
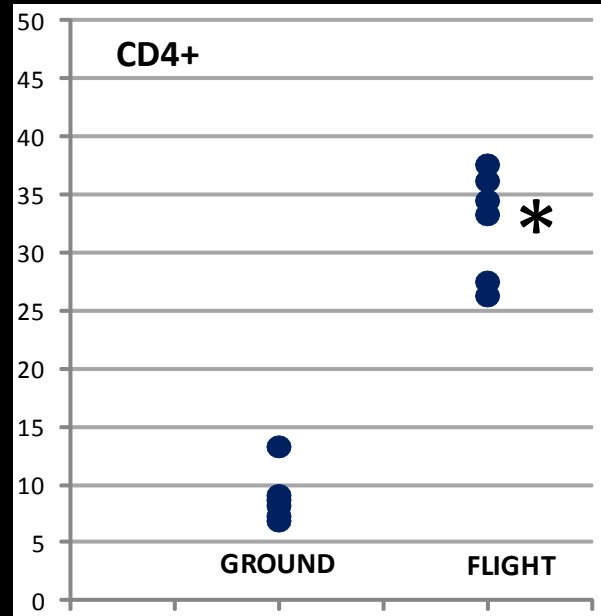
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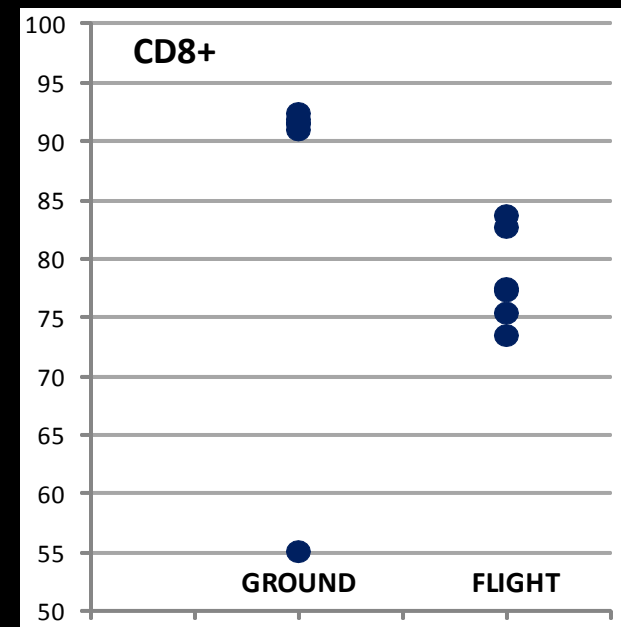
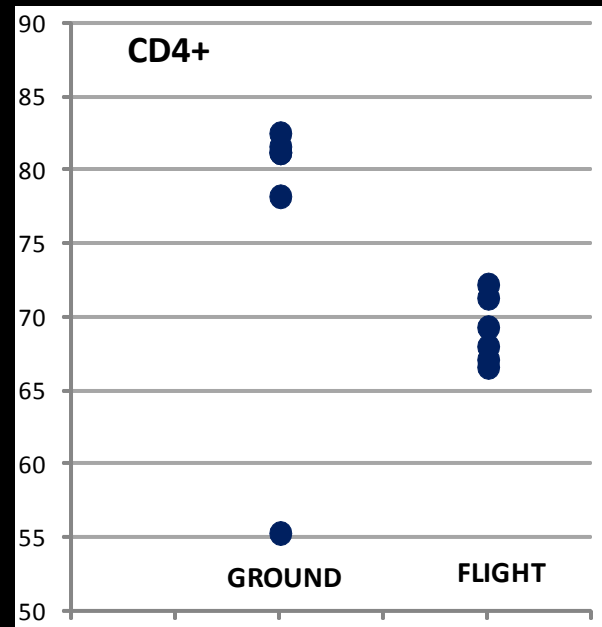
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Data – T Cell Function, 24h culture, CD69/25 dual positive

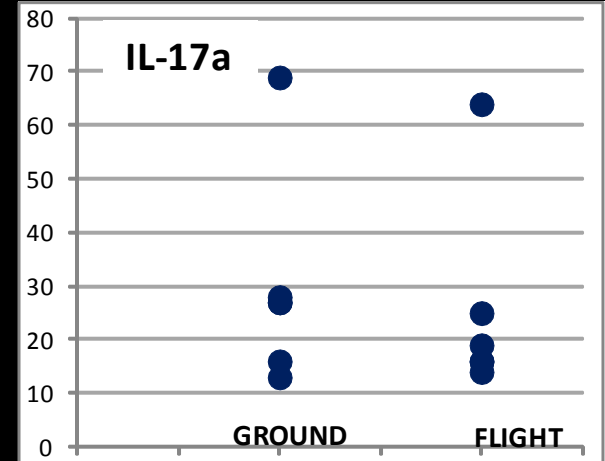
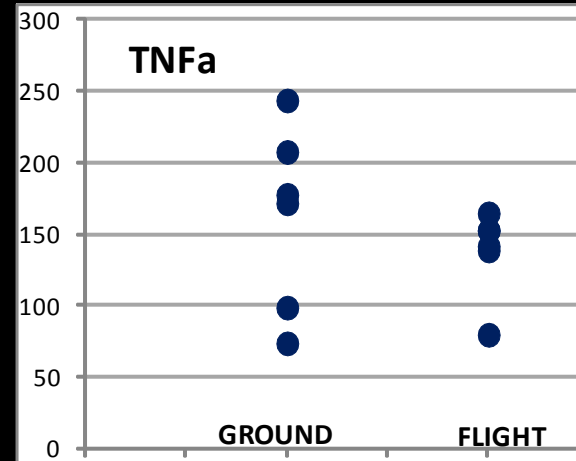
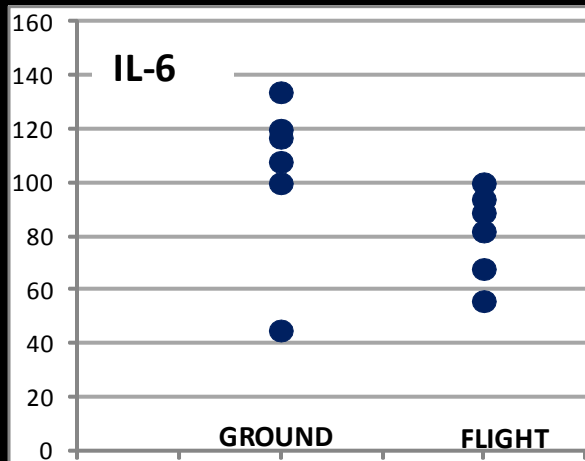
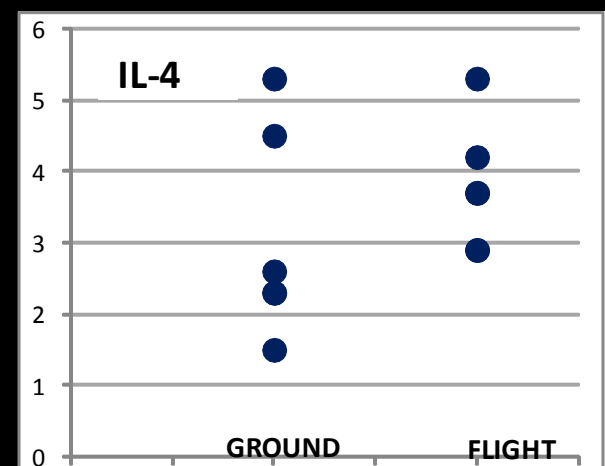
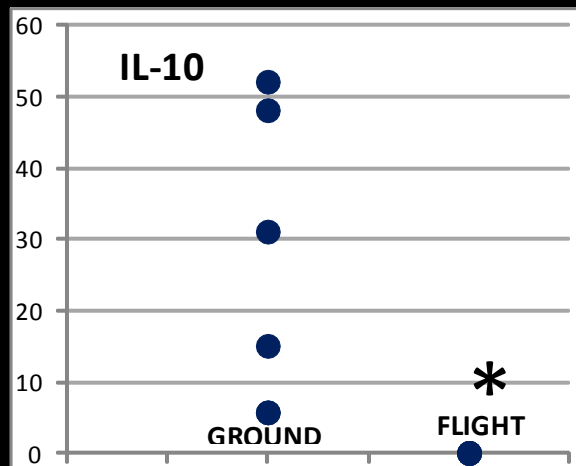
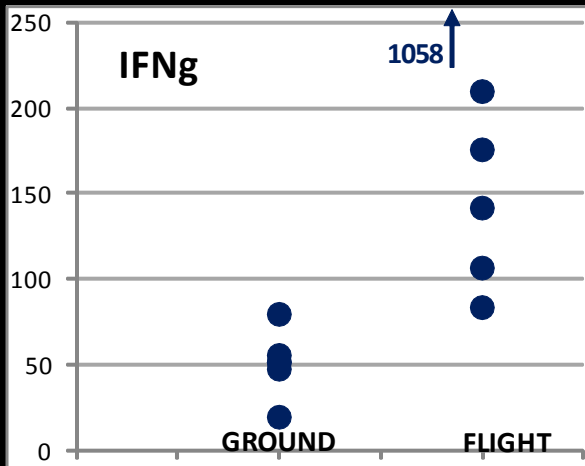
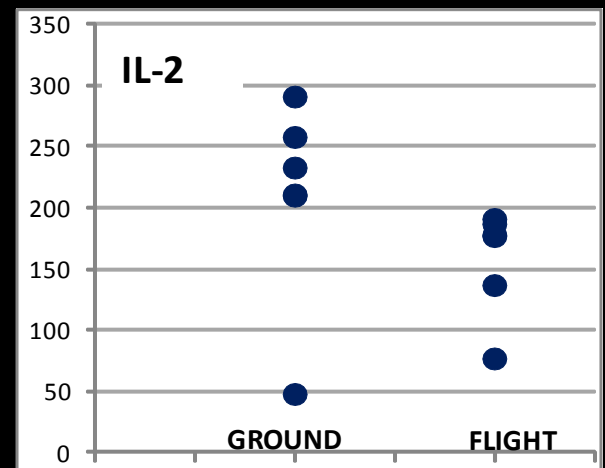
SEA+SEB



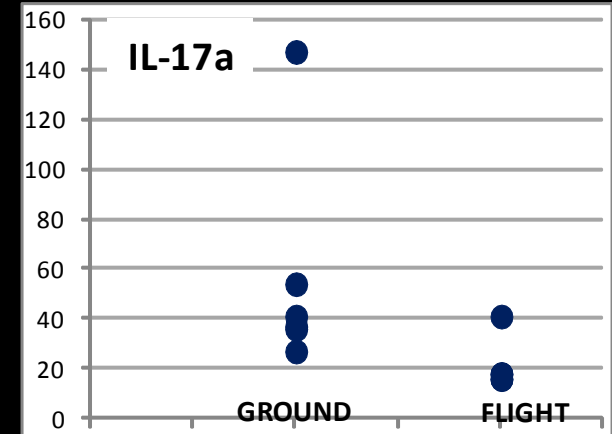
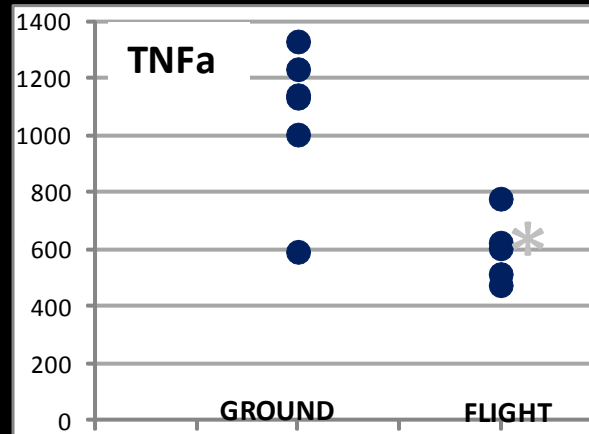
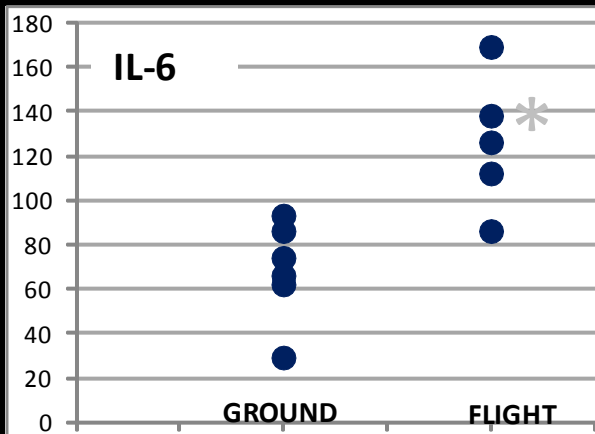
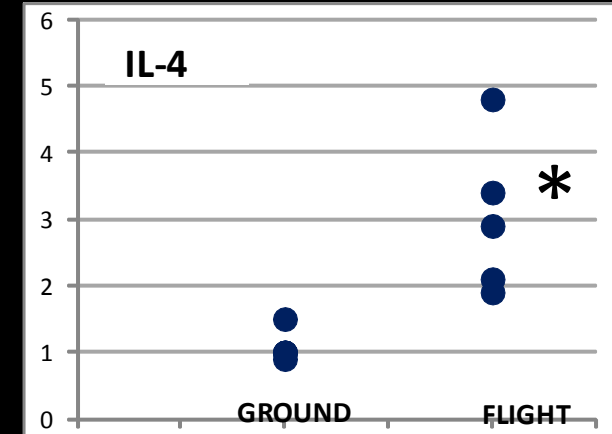
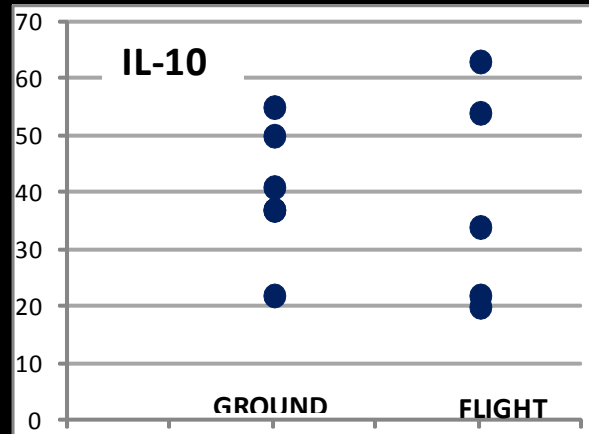
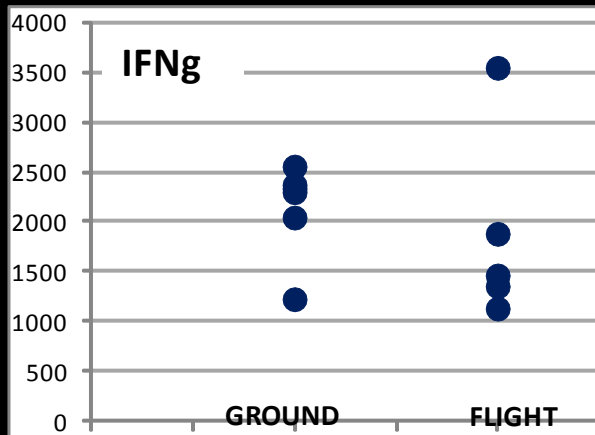
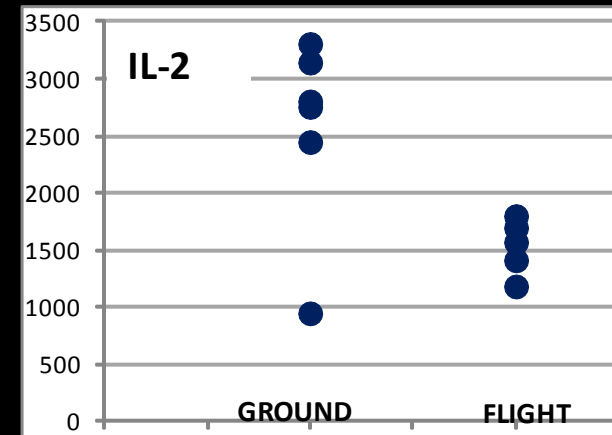
α CD3+CD28



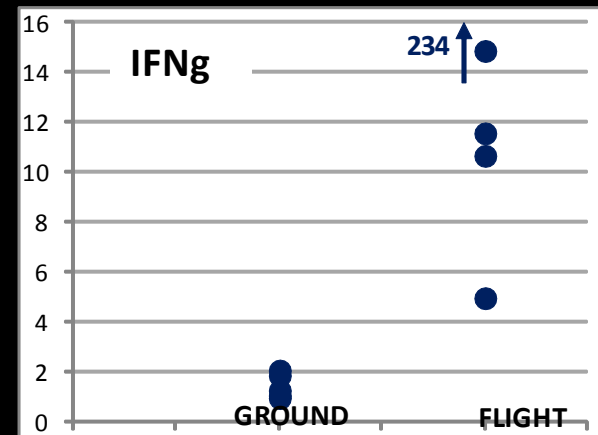
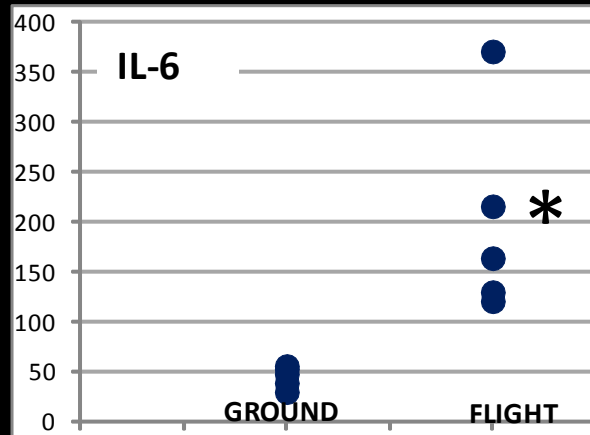
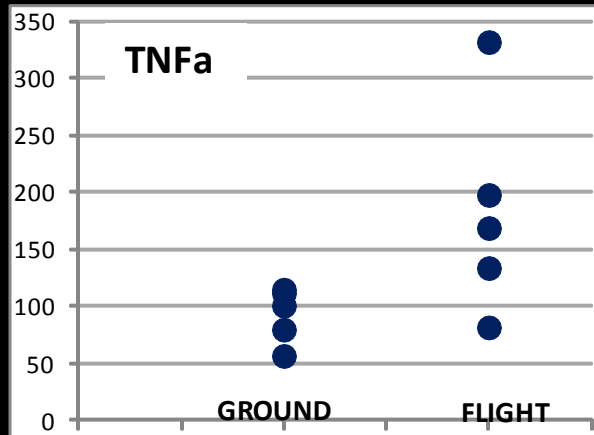
Data – Cytokine Production Profiles (anti CD3/28, 48hr)



Data – Cytokine Production Profiles (anti PMA-I, 48hr)



Data – Cytokine Production Profiles (anti LPS, 48hr)



Conclusions

- These data indicate that alterations in splenocytes phenotype, function and cytokine production patterns are evident following spaceflight.
- The pattern suggests that some innate immune functions are possibly enhanced, whereas some adaptive immune parameters may be inhibited.
- Follow up human and in-flight studies will determine if a clinical risk related to immune dysregulation exists for astronauts.

Acknowledgement:

The Amgen logo, consisting of the word "AMGEN" in a bold, blue, sans-serif font, with a registered trademark symbol (®) to the upper right of the "N". The logo is set against a white rectangular background.

AMGEN®